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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/277,229	03/26/1999	MARTIN CITRON	A-581	3236
21069	7590	12/09/2005	EXAMINER	
AMGEN INC. MAIL STOP 28-2-C ONE AMGEN CENTER DRIVE THOUSAND OAKS, CA 91320-1799			RAO, MANJUNATH N	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/277,229

Applicant(s)

CITRON ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 September 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-14 and 22-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-14 and 22-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>12-17-05</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 11-14, 22-28 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 9-16-05, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Biological Deposit

Examiner notes that applicants have amended claim 11 to recite the ATCC Deposit No. 207159. A perusal of the specification indicates that applicants have made two deposits of plasmids pBSec-Fc and pBSec as follows (see page 77 of the specification). It appears that deposit no. 207158 comprised the polynucleotide encoding the amino acids 1-460 of a (without the transmembrane domain) beta-secretase fused to Fc-portion of human IgG while the deposit no. 207159 comprised a polynucleotide encoding a full length beta-secretase.

15 A plasmid containing cDNA encoding full
length beta secretase has been transformed into in *E.*
coli cells, and the cells have been deposited with the
American Type Culture Collection, 10801 University
Boulevard, Manassas, VA 20110-2209 on March 11, 1999.
20 The cells have been designated as accession no. 207159.
 A plasmid containing cDNA encoding amino
acids 1-460 of beta-secretase fused to the Fc portion
of human IgG beta has been transformed into in *E. coli*
cells, and the cells have been deposited with the
25 American Type Culture Collection, 10801 University
Boulevard, Manassas, VA 20110-2209 on March 11, 1999.
The cells have been designated as accession no. 207158.

However, what is not clear from the support in the specification is that the deposited polynucleotide is indeed SEQ ID NO:1 encoding the polypeptide with SEQ ID NO:4. The above paragraphs found by the Examiner in the specification do not specifically teach that the

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deposited polynucleotide is SEQ D NO:1 encoding the polypeptide with SEQ ID NO:4.

Examiner requests applicants to clarify the above ambiguity.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11, 12, 28 and claims 22-27 depending therefrom are rejected under 35

U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 11, 12 and 28 recite the phrase “polypeptide includes the transmembrane domain”. It is not clear to the Examiner as to what applicants mean by “includes” in the context of the claim. It appears that applicants mean that the “polypeptide comprises the transmembrane domain”. If that is amending the claim accordingly would overcome this rejection.

Claim 12, 27 and claims 26 and 28 depending therefrom are rejected under 35

U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 12, 27 recites the phrase “a nucleic acid molecule”. It is not clear whether said nucleic acid molecules refer to a sequence of nucleotides or just a pair of nucleotides which are also called as “nucleic acid molecule”. Examiner suggests amending the phrase to “**the** nucleic acid molecule” or better “the polynucleotide”. Examiner indeed suggests replacing “nucleic acid molecule” wherever it is recited with “polynucleotide”.

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Claims 12, 25 and claims 26-28 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 recites the phrase “as set forth in”. The metes and bounds of the phrase is not clear to the Examiner. It is not clear whether “set forth in” refers to a specific sequence or a representative sequence. In order to reduce the confusion, Examiner suggests deletion of the phrase and making a direct reference to the SEQ ID NO. such as “polynucleotide sequence SEQ ID NO:1”.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 is directed to polypeptide selected from the groups consisting of fragments of SEQ ID NO:2. Claim 14 is rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:2 including modified polypeptide sequences, modified by at least one deletion, of an amino acid residue in SEQ ID NO:2 and fragments of SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences

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derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov. Reiterating the function of the polypeptide would simply overcome this rejection.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 11-14, 22-28 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gurney(a) et al. (US 6,825,023 B1, 11-30-04, filed 4-12-00, priority date 9-24-1998). Claims 11-14, 22-28 are drawn to an isolated biologically active β -secretase polypeptide selected from the group consisting of the polypeptides with SEQ ID NO:4, or fragments thereof, or a polypeptide with SEQ ID NO:4 but having 1-50 conservative amino acid changes, wherein said polypeptide comprises the transmembrane domain and wherein the polypeptide is encoded by a polynucleotide sequence with SEQ ID NO:1 or fragments thereof, or polynucleotides with conservative changes of 1-50 in the nucleotides of SEQ ID NO:1. Gurney et al. disclose a polypeptide with SEQ ID NO:4 which is 100% identical to the polypeptide with SEQ ID NO:4 of the instant application (see enclosed sequence alignment) comprising the transmembrane domain. The above reference also discloses polynucleotide which encodes polypeptide SEQ ID NO:4, thereby anticipating the polypeptide and its fragments claimed in claims 11-14, 22-28. However, Gurney et al. do not claim an identical polypeptide. The polypeptide claimed by Gurney et al. lacks the transmembrane domain and requires that the claimed polypeptide be at least 90% identical to SEQ ID NO:4.

Therefore in the alternative Examiner takes the position that Gurney et al. renders the invention obvious. Gurney et al. teach a polypeptide with SEQ ID NO:4 which is 100% identical to the polypeptide with SEQ ID NO:4 of the instant application (see enclosed sequence alignment). The above reference also discloses polynucleotide which encodes polypeptide SEQ ID NO:4. However, the claimed polypeptide does not comprise the transmembrane domain as opposed to the polypeptide claimed herein which does comprise the transmembrane domain.

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With the reference of Gurney et al. in hand, it would have been obvious to those skilled in the art specifically interested in making a membrane bound beta-secretase polypeptide to leave the polynucleotide sequences encoding the transmembrane domain in the coding sequences and make a recombinant protein bound to membrane fractions. One of ordinary skill in the art would have been motivated to do so in order to separate the beta-secretase protein from all the soluble cellular proteins. One of ordinary skill in the art would have a reasonable expectation of success since Gurney et al. provide a polynucleotide sequence encoding the full length polypeptide.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office action in which a rejection was made using US Patents granted to Gurney et al. having the filing and priority dates as in the instant rejection, applicants have filed a Declaration under Rule 1.131, swearing behind the date of the previous references. Applicants continue to maintain, since they are swearing behind the reference date and since Gurney et al. do not claim a polypeptide comprising the transmembrane domain, Examiner needs to withdraw the rejection and there is no reason for establishing any interference proceedings as well. Examiner respectfully disagrees. According to 37 CFR 41.023(a), interfering subject matter is that subject matter of a claim of one party which would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa. Since Examiner has now shown that instant claimed subject matter would have been obvious to the party of the instant application in view of Gurney et al., a potential interference situation exists. Examiner suggests that applicants address the above rejections and bring all claims to the

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condition of allowance and proceed with a request for an interference pursuant to 37 CFR

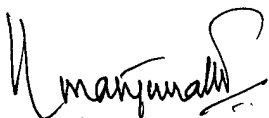
41.202(a). Furthermore, applicant must comply with the requirements set forth in 37 CFR

41.202(a) 2-(a) (6).

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
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December 7, 2005